REMARKS

35 USC 101 Rejection

The Examiner has rejected claims 1-8 and 22-23 (now renumbered as 23-24) under 35 USC 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility, or in the alternative, a well-established utility. The Examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter.

The Applicants do not agree with the Examiner's position. The Applicants assert a utility that is specific, substantial and credible, which is sufficient to meet 35 USC 101 requirements. The Applicants have provided substantial evidence that the claimed composition is a CNS stimulant which when administered to an individual in need is likely to cause fewer unwanted side effects compared with other CNS stimulants. The individual in need would be a person with a condition or disease that could be treated or benefit from the administration of a CNS stimulant.

Evidence of a biological activity of the compound will be relevant to the asserted therapeutic use if there is a reasonable correlation between the activity and the asserted use. *Cross v. Itsuka*, 753 F.2d 1040, 224 USQ739 (Fed Cir 1985). In this case, the evidence of biological activity of the claimed invention is very well correlated to the therapeutic effect. It is well known, that substances classified as a central nervous system stimulant induce an increase in spontaneous locomotor activity (See, for example, Antoniou et al, *Neurosci. Biobehav. Rev.* 23:189-196 (1998), *Principles of Neuropsychopharmacology, Stimulants: Amphetamines and Cocaine* pp 549-590 by Feldman et al., Sinauer Associates, Sunderland, MA 1997) and www.cerb.fr/Snc.htm). In this case (R,R'), (R,S')-amphetaminil showed an increase in spontaneous locomotor activity compared with the racemate and would be useful as a CNS stimulant.

Stereotypy in animal models is indicative that adverse side effects, such as movement disorders, will be associated with the administration of a drug (Roffman and Raskin, *Pharmacol. Biochem. Behav.* 58, 1095-1102 (1997). Furthermore, there may be a correlation between stereotyped behavior observed with amphetamine at high doses in animals and psychosis observed in patients at high doses or chronic use (Randrup and Munkvad *J. Psychiatric Res.* 11:1-10 (1974)). Observation of a decrease in stereotypy implies fewer or less severe side effects. In this case (R,R'),(R,S')-amphetaminil showed a decrease in stereotypy and an increase in the ratio of locomotor activity to stereotypy when compared with amphetamine or the racemic amphetaminil.

Thus, (R,R'),(R,S')-amphetaminil would be a preferred CNS-stimulant compound to administer to minimize the chance or severity of side effects, such as movement disorders or psychosis.

In addition, there is the structural similarity of the claimed compound to compounds which are known CNS stimulants. (R,R'), (R,S')-amphetaminil is one of the isomers derived from racemic amphetaminil which is a known CNS stimulant. Amphetamine, a well known CNS stimulant is also structurally related to (R,R'), (R,S')-amphetaminil. The surprising feature of the claimed invention is the fact that fewer or less severe side effects may be observed when the claimed invention is administered compared with racemic amphetaminil and amphetamine.

The Applicants furthermore provide a non-exhaustive list of conditions or diseases which are known to be improved or treated by the administration of a CNS stimulant. The conditions or diseases listed here include and expand on those conditions and diseases listed in the patent application. These conditions and diseases include: Parkinson's (Miller and Nieburg, *NY State J. Med.* 73:2657-61 (1973), Yahr and Duvoisin, *N. Engl. J. Med.* 287:20-4 (1972)), depression (Little, *J. Clin. Psychiatry* 54:349-55(1993), Olin and Masand *Psychosomatics* 37:57-62 1996), depression and fatigue (Wagner and Rabkin, *J. Clin. Psychiatry* 61:436-40(2000)), potentiating the effect of an antidepressant (Masand, et al. *Depress. Anxiety* 7:89-91 1998, Fawcett et al. *J. Clin. Psychopharmacol.* 11:127-32 (1991)), apathy (Marin et al. *J. Neuropsychiatry Clin. Neurosci.*, 7:23-30 (1995)), poststroke symptoms of apathy and depression (Robinson and Bloom *Biol. Psychiatry.* 12:669-80 (1977)), hypotension (Susmano et al. *Pacing Clin. Electrophysiol.* 16:1235-9 (1993)) hypotension and bradycardia (Grubb et al. *Pacing Clin. Electrophysiol.* 19:836-40 (1996)), potentiating opiod analgesia (Yee and Berde *J. Pain Symptom. Manage.* 9:122-5 (1994)), pain control in advanced and recurrent head and neck cancer (Shapshay et al. *Otolaryngol. Clin. North Am* 13: 551-60 (1980)), in cancer care (Homsi et al. *Support Care Cancer* 8:385-97 (2000) and Rosenfeld and Broder *Cancer Treat Rep.* 68:659-60 (1984)) attention deficit hyperactivity disorder (ADHD), narcolepsy, impulsivity, inattention and hyperactivity (www.health.enotes.com/neurological-disorders-encyclopedia/central-nervous-system-stimulants), nasal decongestant, analeptic, obesity, reversing the effects of fatigue, sleeping disorders (www.answers.com/topic/amphetamine), obesity and hypersomnolence (Ismail et al, *J. Pediatr. Endocrinol. Metab.* 19:129-34 (2006)), obesity and hyperphagia (Mason et al. *Arch. Pediatr. Adolesc. Med.* 156: 887-92 (2002).), recovery from stroke (Walker-Batson et al. *Stroke* 26:2254-9 (1995)), memory retention (Lee and Ma *Brain Res,. Bulletin* 37:411-16 (1995), memory enhancement (M'Harzi et al. *Physiology and Behav* 42:575-579 (1988)), hyperactivity (Brown et al. *Psychopharmacol.* 62:133-14 (1979)) narcolepsy (Parkes and Fenton, *Neurology, Neurosurg. Psychiatry* 36:1076-1081 (1973)), Alzheimer's disease (Filip and Kolibas *J. of Psychiatry and Neursci* 23:234-243 (1999), Tariot et al. *Phsychopharmacol.* 91:489-495 1987),

and renal disease (Bett *Postgrad. Med. J.* 22: 205-18 (1946)), and nicotine withdrawl (Prignot *Eur. Respir J.* 2:550-60 (1989)).

Since these conditions or diseases are known to be treated or improved by a CNS stimulant, the Applicants believe that the claimed invention, a CNS stimulant, would be useful to treat or benefit the same conditions or diseases. Applicants believe that an adequate link has been provided between the evidence of record and the claimed invention. The invention provides a novel composition which acts as a CNS stimulant and that surprisingly shows potentially fewer or less severe side effects, such as movement disorders, based on animal studies that show an increased locomotor/ stereotypy activity ratio compared with racemic amphetaminil.
Claims 1-8 and 23 and 24 are in condition for allowance.

35 USC 112, First Paragraph, Rejection

The Examiner has rejected claims 22-23 (now renumbered as claims 23-24) under 35 USC 112, first paragraph, as failing to comply with the written description requirement. The Examiner states that it is not clear which disorders or conditions would be known to benefit or be treated by a CNS stimulant at the time of filing of the patent application.

Applicants believe that the language "the treatment of a condition or disease benefiting from or requiring a central nervous system stimulant" is sufficiently described in the patent application. For example in paragraph [0023] , the claimed composition is said to be useful "for the treatment of a number of conditions and diseases for which racemic amphetaminil, as well as other related compounds including amphetamine, and in particular D-amphetamine, have been used therapeutically". The central nervous system stimulant referred to in the claims is the same as any of those described in paragraph [0023] and would be understood to be so from the disclosure of the patent application. Inclusion of the non-exhaustive list of conditions or diseases in paragraph [0024] further clarifies the type of conditions and disorders that would benefit from the claimed invention. The Applicants have also expanded on the list identifying additional conditions or diseases benefiting from a CNS stimulant above to show that a large number of conditions and disorders are treatable with the claimed invention and were known prior to filing the instant patent application. Remarkably, the uses described by Applicants were reviewed in 1946 by Bett (Bett *Postgrad. Med. J.* 22: 205-18 (1946)). Amphetamine, one of the compounds related to the claimed invention and described in the article by Bett, was first synthesized in 1927 and used first as a nasal/bronchial decongestant and for asthma. Other uses are described in the article as well

including narcolepsy, Parkinson's, fatigue and depression, substance abuse, hyperactive children, obesity and the like.

Furthermore, Applicants have amended claims 23 and 24. In view of the remarks and amendments to claim 23 and 24, the claims are now in condition for allowance.

The Applicants kindly request the present claims be allowed

Any questions about this response should be addressed to Karen Guerrero and the telephone number is 610-933-2490.

Sincerely,

Karen Guerrero

Karen Guerrero
Registration No. 37,071